REMARKS

The Office Action mailed July 1, 2008 has been carefully considered and the following response prepared.

Claims 1-36 are pending in the application. Claims 8, 13-22, 29 and 33-36 are withdrawn from consideration. Claims by combining claims 9 and 11 with claim 1, and claim 1 has been rewritten as new independent claim 41. In new claim 41, the definitions of R^1 and R^2 have been amended such that R^1 and R^2 are each H. Claims 6, 7, 10, 12, 39, and 40 have been amended to change the dependency to new claim 41. Claims 1, 9 and 11 have been canceled without prejudice. No new matter has been added.

Applicants' representative, Liza D. Hohenschutz, would like to thank Examiner Andrew Kosar for the very helpful and courteous telephone interview on October 15, 2008 during which the rejections in the Office Action mailed July 1, 2008 and proposed amendments to the claims were discussed. Examiner Kosar indicated that a proposed claim, corresponding to new claim 41, which combines the subject matter of claims 1, 9 and 11, would likely be allowable. The substance of the interview will be discussed in more detail in connection with Applicants' response to the rejections below.

Rejections under 35 USC 103

At page 3 of the Office Action, the Examiner rejected claims 1-4, 6, 7, 12, 23-25, 27, 28, 30-32, 39 and 40 under 35 USC 103 as unpatentable over Smales et al., *Journal of Chemical Education*, Vol. 76, No. 11, pages 1558-1560, 1999, in view of Schäfer, Swiss patent CH-640 511, Saha et al, *Tetrahedron Letters*, Vol. 36, No. 21, pages 3635-3638 (1995) and Mimura, U.S. Patent No. 6,197,998. At page 6 of the Office Action, the Examiner rejected claims 1-4, 6, 7, 9-12, 23-25, 27, 28, 30-32, 39 and 40 under 35 USC 103 as unpatentable over Smales et al., Journal of Chemical Education, Vol. 76, No. 11, pages 1558-1560, 1999, in view of Schäfer, Swiss patent CH-640 511, Saha et al, *Tetrahedron Letters*, Vol. 36, No. 21, pages 3635-3638

(1995) and Mimura, U.S. Patent No. 6,197,998, and further in view of Anteunis (U.S. Patent 4,723,645).

Applicants traverse these rejections. Both rejections were discussed during the telephone interview with Examiner Kosar on October 15, 2008. During the telephone interview, proposed amendments to the claims, as shown in new claim 41, were discussed. New claim 41 combines claim 1 with claims 9 and 11, and amends the definition of R^1 and R^2 such that R^1 and R^2 are each H. Claims 1, 9 and 11 are canceled without prejudice. Examiner Kosar advised Applicants representative that it is likely that new claim 41 would be allowable. The prior art cited in the rejections was also discussed.

For some uses of peptides, such as medicinal products, intermediates for producing peptides, and as spacer arms in pharmaceutical compositions that target active compounds to specific cells in the body, peptides of high optical purity are very desirable. Synthesis of peptides from amino acids using methods known in the art requires many protection, deprotection and coupling reactions, during which racemization of the peptide may occur.

Applicants found surprisingly that the method according to the invention makes it possible to obtain, with high preparative yield, complex peptides exhibiting several stereogenic centers, while at the same time avoiding racemization. The peptides produced by the claimed methods exhibit high optical purity.

There is no disclosure or suggestion in the combined teachings of the cited references of methods of that can produce peptides comprised of at least two enantiopure amino acids and glycine, as claimed by Applicants.

Smales et al. discloses the peptide Gly-Phe-Leu-Gly and its synthesis using a method that is different than the claimed methods, as noted by the Examiner. Applicants again submit that Smales et al. is not relevant to the claimed methods, as it does not disclose any of the steps of the claimed methods.

Schäfer was discussed at length during the interview. Schäfer discloses synthesis of trishydroxymethylmethane-substituted lower peptides. In the method disclosed therein, trishydroxymethylaminomethane is reacted with N-(2-haloacetylated) amino acids or N-(2-haloacetylated) di-, tri- and tetrapeptides of the formula X-CH_2-C(O)-Y, where X is Cl, Br or I, and Y is an amino acid or a di-, tri- or tetrapeptide. Example 3 of Schäfer discloses preparation of Tris-Gly-Gly-Arg-Ser-Threo. In Example 3, N-2-Br-acetyl-l-gly-l-arg-d-asp-l-threo (K salt) is with mixed with trishydroxymethylaminomethane and heated to boiling under reflux with exclusion of light for 45 minutes. The stereochemistry of the product, Tris-Gly-Gly-Arg-Ser-Threo, is not mentioned. The absence of designations of stereochemistry would be understood by persons skilled in the art as meaning that all of the amino acids in the peptide have the l configuration, and that the process in Example 3 results in racemization of the peptide product. The result apparently obtained from the process of Example 3 is directly opposite to the result obtained with the claimed methods. The claimed methods avoid racemization of the peptide product. Persons skilled in the art would not look to the process of Schäfer for preparing peptides comprised of at least two enantiopure amino acids and glycine.

Saha et al. discloses synthesis of N-linked-glycopeptoids. In Scheme 2, N-substituted glycine building blocks were prepared from t-butyl bromoacetate to which was added a primary amine to form leucine, phenylalanine and alanine analogues. Dipeptoid units were formed by coupling the glycine building blocks with an N-acetylglucosamine substituted amine. Some of the steps of the synthetic scheme were carried out at 0°C. The dipeptoid unit was further elongated by treatment with acid. Applicants again submit that Saha et al. is also not relevant to the claimed methods. The methods in Saha et al. produce a peptoid based on glycine that has no chiral centers, rather than a peptide as produced by the claimed methods.

Mimura discloses synthesis of glycyl-tyrosine using chloroacetyltyrosine and aqueous ammonia (Example 2, column 5). The reaction was carried out at a temperature of 40°C. There is no disclosure or suggestion in Mimura of preparing longer peptides.

There is no disclosure or suggestion in the combined teachings of the cited references, or the knowledge of persons skilled in the art, of the claimed method for preparing a peptide or a

peptide derivative comprising at least two enantiopure amino acids and at least one glycine molecule. Smales et al. and Saha et al. are not relevant to the claimed methods. The method of Schäfer is carried out at a much higher temperature than the claimed methods, apparently leading to racemization of the product, and producing a different product than the claimed methods. There is no indication of how the process in Mimura could be used to produce enantiopure peptides, or whether it would even be possible to produce enantiopure peptides using the method disclosed in Example 2 of Mimura. The combined teachings of the cited references fail to teach or suggest a method for preparing peptides comprising at least two enantiopure amino acids and glycine as claimed in the methods of the invention. Persons skilled in the art would have no motivation to combine the teachings of the prior art in the manner suggested by the Examiner, nor would they have a reasonable expectation of successfully producing such peptides.

In contrast to the teachings of the cited references, the methods of the invention make it possible to obtain, with a high preparative yield, complex peptides exhibiting several stereogenic centers, while at the same time avoiding racemization. Claims 2-4, 6, 7, 12, 23-25, 27, 28, 30-32, 39, 40, and new claim 41 are therefore not obvious in view of the combined teachings of Smales et al., Schäfer, Saha et al. and Mimura.

Anteunis et al. is concerned with the preparation of peptides that uses a coupling reaction wherein the amino acid reactants are activated with trialkylsilanes that facilitate the formation of peptide bonds. There is no suggestion or disclosure of step (b) of claim 41, reacting the compound of general formula (II) as defined in step a) with a compound of general formula HNR^1R^2 (III) in which R^1 and R^2 are each H, wherein the reaction is carried out at a temperature of -30°C to +60°C. Anteunis et al. therefore adds nothing to the teachings of Smales et al., Schäfer, Saha et al. and Mimura that would render obvious the methods of claims 2-4, 6, 7, 10, 12, 23-25, 27, 28, 30-32, 39, 40, and new claim 41.

Claims 2-4, 6, 7, 12, 23-25, 27, 28, 30-32, 39, 40, and new claim 41 are not obvious over the combined teachings of Smales et al., Schäfer, Saha et al. and Mimura. Claims 2-4, 6, 7, 10, 12, 23-25, 27, 28, 30-32, 39, 40, and new claim 41 are not obvious over the combined teachings

of Smales et al., Schäfer, Saha et al., Mimura, and Anteunis. Withdrawal of both section 103 rejections is respectfully requested.

In view of the above, the present application is believed to be in a condition ready for allowance. Reconsideration of the application is respectfully requested and an early Notice of Allowance is earnestly solicited.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 03-2775, under Order No. 05129-00072-US. A duplicate copy of this paper is enclosed.

Respectfully submitted,

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By /Liza D. Hohenschutz/

Liza D. Hohenschutz
Registration No.: 33,712
CONNOLLY BOVE LODGE & HUTZ LLP
1007 North Orange Street
P.O. Box 2207
Wilmington, Delaware 19899
(302) 658-9141
(302) 658-5614 (Fax)
Attorney for Applicant

595606